article, "Ageing human bone: factors affecting its biomechanical properties and the role of collagen" published in the Journal of Biomaterials (applied) (2001) 15, 187-231). Furthemore, a value of about 1 kJ m^{-3} for the toughness of bone was provided in studies conducted by Ashby, M F; Gibson, L J; Wegst, U; and Olve, R. in their metanalysis published in Proceedings of the Royal Society, Mathematical and Physical Sciences (1995), 450, 123-140. Thus a target compressive toughness of 1.3 kJ m^{-3} measured by the J-integral method is appropriate for load-bearing BRMs.

[0017] The compressive strength of normal human cancellous bone shows considerable variation, but typically is about 5 MPa, though may fall beneath 2 MPa in osteoporotic bone (Togawa, D. Kayanja, M. M., and Lieberman, I. H. (2005), "Percutaneous Vertebral Augmentation" in The Internet Journal of Spine Surgery 1, (2), http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijss/vol1n2/vertebral.xml).

[0018] Cortical bone, with a compressive strength of about 10-160 MPa, is considerably stronger than cancellous bone (Cowin, S. Ed (1989) "Bone Biomechanics". CRC Press, Boca Raton and by Duck, F. A. (1990) "Physical Properties of Tissue: A comprehensive Reference Book", Academic Press, London). Although cortical bone is often much thinner than the underlying trabecular bone, it makes a significant contribution to the mechanical properties of whole bone, accounting for approximately 60% of the bending strength in the femoral neck and about 10% of the compressive strength of vertebral bodies (Werner et al., 1988). Thus a target compressive strength of about 20 MPa is appropriate for load bearing BRMs.

[0019] An approximate match between the compressive elastic modulus of a BRM and bone is also important to prevent high stress accumulation and stress shielding. Cortical bone has an elastic modulus of 12-18 GPa while that for cancellous bone is 0.1-0.5 GPa (Rezwana, K.; Chena, Q. Z.; Blakera, J. J.; Boccaccini, A. R., (2006), "Biodegradable and bioactive porous polymer/inorganic composite scaffolds for bone tissue engineering." in Biomaterials, 27 3413-3431). As most of an implant of a BRM will be in contact with cancellous bone rather than cortical bone, a compressive elastic modulus of 0.1-0.5 GPa is an appropriate target for BRMs.

[0020] Solid hydroxyapatite, bioglass or glass-ceramic mixtures are considerably stiffer than bone, while porous hydroxyapatite is considerably less stiff, as disclosed by Rezwana, K (2006) op. cit.

[0021] It is generally understood that mineral density is a major determinant of compressive strength and compressive elastic modulus in mineralized composites. Thus, the compressive strength and compressive elastic modulus of trabecular bone increases approximately with the square of its density (Carter, D. R. and Hayes, W. C., (1976) in the article "Bone compressive strength: the influence of density and strain rate" published in Science 194, 1174-1176). This may also be true for ceramic and for mineral-containing composite BRMs. Thus, it is highly desirable from a mechanical perspective that composite BRMs are heavily mineralised.

[0022] In addition to the requirement that the mechanical properties should match those of the bone, BRMs need to be osteoconductive. Osteoconductivity is generally defined as the process by which osteogenic cells migrate to the surfaces of a material through the fibrin clot established immediately after implantation of a BRM. This migration of osteogenic cells through the clot causes retraction of the temporary fibrin matrix. Hence, it is important that the fibrin matrix is well secured to the material, because if it is not, when osteogenic cells start to migrate along the fibrin fibres, wound contraction can detach the fibrin from the material. It has been previously shown that a rough surface will bind the fibrin matrix better than a smooth surface and hence will facilitate the migration of osteogenic cells to the surface of the material.

[0023] Therefore, it is generally accepted that the factors that are important for osteoconductivity are as follows:

[0024] (i) an open porous structure with pores of sufficient size to allow the migration of bone-forming cells, whilst preventing the migration of other tissues and unwanted cell types;

[0025] (ii) provision of some pores of sufficient size to allow for the inward migration of blood vessels;

[0026] (iii) maintenance of a suitable vascularised environment for bone cell differentiation;

[0027] (iv) provision of a suitable surface for bone cells adhesion and function; and

[0028] (v) a rough surface to bind the fibrin matrix.

[0029] Thus, a porous structure is highly desirable to enable cells and new vessels to colonise the interior of the porous BRM. The minimum pore size to permit cellular ingress is considered to be 100 μm, but pore sizes of 300 μm may enhance vascularisation and new bone formation and smaller pores favor hypoxic conditions and cartilage formation before osteogenesis (Karageorgiou, V.; Kaplan, D. (2005), "Porosity of 3D biomaterial scaffolds and osteogenesis" in Biomaterials, 26, (27), 4745491). However, greater pore size and porosity have a negative effect on the compressive strength, compressive elastic modulus and compressive toughness of a BRM.

[0030] A range of methods have been used to produce intercommunicating pores in materials including thermally induced phase separation, freezing, solvent casting, particle leaching, supercritical gas foaming, incorporation of resorbable monofilaments, sintering of microsphere and solid free form coating. Many proposed BRMs either lack pores completely or have pores of an inappropriate size for optimal osteoconductivity.

[0031] Osteoinductivity is generally defined as the ability to induce non-differentiated stem cells or osteoprogenitor cells to differentiate into osteoblasts. The simplest test of osteoinductivity is the ability to induce the formation of bone in tissue locations such as muscle which do not normally form bone (ectopic bone growth). Some allograft substitutes are osteoinductive, probably on account of the bound growth factors. Some calcium phosphate minerals are osteoinductive possibly because they adsorb and concentrate bone growth factors from tissue fluids. It is generally understood that a variety of BRMs can be made osteoinductive by adding growth factors such as rhBMP-2 to them.

[0032] It is generally understood that it is highly desirable that BRMs are fully resorbable to allow entire BRM replacement with endogenous tissue. It is also generally understood that in a load bearing BRM, the half-resorption time needs to be fairly slow, probably about 9 months, to allow time for the replacement tissue to acquire full strength and toughness to take over load-bearing from the BRM. Synthetic polymers based on monomers of lactic acid, glycolic acid, dioxanone, trimethylene carbonate and caprolactone, or a combination of these monomers resorb too quickly and have acidic breakdown products which may be irritants.

[0033] Currently there are no existing products on the market that fulfill the main criteria for the ideal BRM as stated by